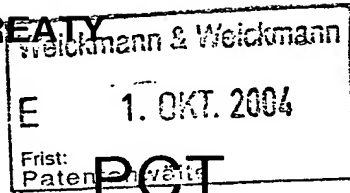


PATENT COOPERATION TREATY



From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/004345

International filing date (day/month/year)
23.04.2004

Priority date (day/month/year)
23.04.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/35, C07K14/195

Applicant
MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/004345

B x No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/004345

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-38
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-38
Industrial applicability (IA)	Yes: Claims	1-38
	No: Claims	

2. Citations and explanations

see separate sheet

Ad Section V: Reasoned statement with regard to novelty, inventive step or industrial applicability

1) Documents

D1...WO 99 10496

D2...Reyrat et al. (1995) PNAS 92: 8768-8772

D3...Reyrat et al. (1996) Infection and Immunity 64: 3934-3936

2) Novelty and inventive step

The present application relates to a urease deficient cell which comprises a recombinant nucleic acid molecule encoding a fusion polypeptide comprising a domain from a polypeptide capable of eliciting an immune response in a mammal and a phagolysosomal escape domain and its application as vaccine.

The claims are considered to meet the requirements of Art. 33(2) PCT as the prior art does not disclose a cell as defined in the claims.

Claims 1-38, however, are not considered to meet the requirements of Art. 33(3) PCT for the following reasons:

D1 is considered to represent the closest prior art. D1 discloses a tuberculosis vaccine comprising as an active agent a cell comprising recombinant nucleic acid molecule encoding a fusion polypeptide comprising a domain from a polypeptide capable of eliciting an immune response in a mammal and a phagolysosomal escape domain.

The difference between the bacterial cell/vaccine disclosed in D1 and that of the present application lies in the fact that the cell of the present application is additionally required to be urease deficient.

The problem to be solved by the present application, thus can be seen in the provision of a bacterial cell useful for vaccination purposes which exhibits an increased safety profile.

Urease has long been discussed to contribute to bacterial virulence (D2, p. 5651,

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/004345

p. 5651, right col., 2nd full par.; D3, p. 3934, left col., 1st par.).

The provision of a urease-deficient bacterial cell as defined in claims 1 and 17 as well as methods for preparing such cells or their application as vaccines cannot be considered to involve an inventive step.